DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

December 20, 2014

Horiba ABX SAS/Horiba Medical
c/o Ms. Caroline Ferrer, Regulatory Affairs Manager
Parc Euromedecine
Rue du Caducee - BP7290
34184 Montpellier Cedex 4 - France

Re: k141161
Trade/Device Name: ABX Micros ES 60 OT and ABX Micros ES 60 CT
Regulation Number: 21 CFR 864.5220
Regulation Name: Automated differential cell counter
Regulatory Class: Class II
Product Code: GKZ
Dated: November 14, 2014
Received: November 17, 2014

Dear Ms. Ferrer:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Leonthena R. Carrington -A

for Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k141161

Device Name
ABX MICROS ES 60 OT (Open Tube model)
ABX MICROS ES 60 CT (Close Tube model)

Indications for Use *(Describe)*
The ABX MICROS ES 60 (OT and CT models) is a quantitative multi-parameter, automated hematology analyzer for in vitro diagnostic use in clinical laboratories to identify and enumerate the following parameters: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, PLT, MPV, LYM%, LYM#, MON%, MON#, GRA%, GRA#, in K2EDTA and K3EDTA anticoagulated venous whole blood samples of adult patient population. It is not intended to be used for pediatric subjects.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Premarket Notification [510(k)] Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is : k141161

1.0 Sumitted by :

Company: HORIBA ABX SAS
HORIBA MEDICAL
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2.0 Date Submitted :

14th November 2014

3.0 Device Name and Classification :

Trade/Proprietary Name: **ABX MICROS ES 60**

Classification:

Device:	Counter, differential cell
Panel:	81 Hematology
Regulation number:	864.5220
Product Code:	GKZ
Class:	2

4.0 System description :

4.1 Device Description

The **ABX MICROS ES 60** is a quantitative, automated hematology analyzer and leukocyte differential counter for in vitro diagnostic use in clinical laboratories. The instrument system is comprised of the analyzer and a suite of analytical reagents that allow for simultaneous quantitative determination of hemoglobin measurement, cell counting, quality control, calibration, and cleaning. The system is a microprocessor controlled hematology analyzer used for the in vitro diagnostic testing of whole blood specimens. It operates in complete blood count (CBC) and Differential (DIFF) mode

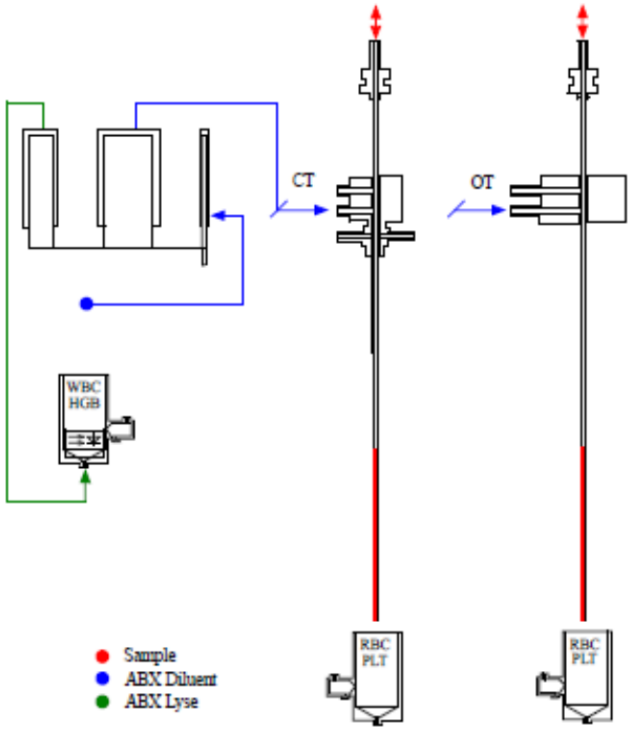
using a combination of focused flow impedance and light transmission technologies. It is available in Closed (CT) or Open Tube (OT) sampling versions.

4.2 Principles of Operation

The ABX Micros ES 60 principle of automated cell counting and sizing is used in the analysis of the whole blood. Each cell suspended in a conductive liquid (diluent) acts as an insulator. As each cell goes through the aperture, it momentarily increases the resistance of the electrical path between two submerged electrodes on either side of the aperture. This causes a measurable electronic pulse. While the number of pulses indicates particle count, the amplitude of the electrical pulse is proportional to the cell volume. These pulses are sent to the Signal Conditioner for analog to digital conversion. Pulse counts and digitized pulse measurements are sent to the System Manager for processing by the algorithms where the reported parameter values, flags and histograms are generated.

The diluted sample is processed through two different chambers:

- The RBC / PLT chamber, for the Red Blood Cell (RBC) and Platelet (PLT) detection
- The WBC / HGB chamber, for the White Blood Cell (WBC) and Hemoglobin (HGB) counts



Red Blood Cells (RBC) and Platelets (PLT) Detection:
The blood specimen is diluted in the electrolytic (current conductor) ABX Minidil LMG and pulled through the 50 µm calibrated micro-aperture in the mini flow-cytometer. Two electrodes are placed on either side of the aperture. Electric current passes through the electrodes continuously. When a cell passes through the aperture, the electric resistance between the two electrodes increases proportionately to the cell volume.
The impedance variation is measured and allows for the RBC and PLT quantification.

Hemoglobin Measurement:
The lysing reagent breaks down the RBC cell membrane and releases the hemoglobin contained by the cell. The hemoglobin, released by the lysing reagent, combines with the potassium cyanide from the lysing reagent to form a chromogenous cyanmethemoglobin compound. This compound is then measured through the optical part of the WBC/HGB chamber by spectrophotometry at a wavelength of 550 nm.

Hematocrit Measurement:
All the RBC pulses are grouped into various sizes. Each group pulse height is then averaged. All the pulse height averages are then averaged one final time for a mean average of all the RBC pulse heights. This function is a numeric integration of the MCV.
The HCT results are given as a percentage of this integration.

Red Distribution Width (RDW) Calculation:
The RDW is calculated from the RBC histogram. It allows to follow the evolution of the width of the RBC histogram in relation to the number of cells and their average volume.

Mean Cell Volume (MCV), Mean Cell Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC) Calculations:
The MCV is calculated directly from the entire RBC histogram. The MCH is calculated from the HGB value and the RBC count. The MCHC is calculated according to the HGB and HCT values.

Mean Platelet Volume (MPV):
The MPV is directly derived from the analysis of the platelet distribution curve.

White Blood Cell (WBC) Count:
The WBC count is carried out in the WBC/HGB chamber. The detection principle is the same as for RBC.

ABX Minidil LMG reagent preserves and prepares the WBC cell membrane for the differential reaction. The lysing reagent has a differential mode of action on the WBC cytoplasmic membranes.

- When the lysing reagent reacts with the lymphocytes, the cytoplasm and the membrane are destroyed. At the end of the lysing action, only the nucleous remains intact and this action results in a smaller volume detected by the instrument.

- When the lysing reagent reacts with the monocyte cytoplasmic membrane, it has an intermediate reaction that empties the cytoplasm from the cell. At the end of the lysing action, the monocyte cells obtained have an intermediate size between the lymphocytes and the granulocytes.
- When the lysing reagent reacts with the granulocytes, it has a limited reaction due to a molecule in their cytoplasmic structure which protects them from the shrinking action of the lyse. This in turn makes the granulocytes the larger of the WBC sub-populations in the cell differentiation.

The three sub-populations of WBCs are placed according to the number of cells and the size of the cells in each group. The lymphocyte, monocyte and granulocyte results are given as a percentage of the entire WBC count.

The granulocytes subpopulation of the WBC contains three sub-populations that contain cytoplasmic granular material which stain various colors when viewed microscopically.
They are as followed:
■ Neutrophils
■ Eosinophils
■ Basophils
The distribution of these cells depends on the pathological and physiological conditions of the individuals analyzed.
Pathological cells are placed in different zones within the WBC distribution curve and trigger alarms.

4.3 Modes of Operation

Two models of ABX Micros ES 60 are available.

- The Closed Tube (CT) instrument: it has a cap-piercing mechanism. The blood collection tube is placed directly in the analyzer without removing the cap.
- The Open Tube (OT) instrument: the cap form the blood collection tube must be removed before analyzing the sample.

4.4 Specimen Identification

Specimen identification is by manual sample identification with the use of a hand held barcode scanner.

4.5 Calibration

Calibration is a procedure that is performed during specific situations such as installation, maintenance or service intervention. It is performed by a HORIBA ABX SAS representative. It ensures that the precision and accuracy of the analyzer are acceptable, so that accurate measurements are performed by the analyzer.

ABX Minocal calibrator (k955925) is used for the ABX Micros ES 60 calibration procedure. Assigned assay values are traceable to reference methods.

4.6 Quality Control

Quality control allows the user to monitor a set of analyses based on known sample values and ranges over a period of several months. Statistical computation performed on these populations allows the extraction of qualitative information related to the stability of the instrument.
ABX Minotrol 16 Control (k850755) enables monitoring of system performance for all directly measured and calculated CBC and Diff parameters. Assigned assay values are determined on validated instruments using the appropriate reagents.

4.7 Software

HORIBA ABX SAS's Hazard Analysis and Software Development process for this product are included in this submission.

5.0 Intended use

5.1 Indications for Use :

The **ABX MICROS ES 60** (OT and CT models) is a quantitative multi-parameter, automated hematology analyzer for in vitro diagnostic use in clinical laboratories to identify and enumerate the following parameters: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, PLT, MPV, LYM%, LYM#, MON%, MON#, GRA%, GRA#, in K2EDTA and K3EDTA anticoagulated venous whole blood samples of adult patient population. It is not intended to be used for pediatric subjects.

5.2 Special Conditions for Use Statements:

For prescription use only

6.0 Substantial Equivalence Information :

The following tables show the similarities and differences between the candidate device and its predicate device identified below.

6.1 Predicate Device Name and 510(k) number:

Candidate device	Predicate device	Manufacturer	510(k) number
ABX MICROS ES 60	ABX MICROS 60	HORIBA ABX SAS	k030799

6.2 Comparison with predicate Device : Similarities

Item	**Candidate (ABX MICROS ES 60)**	**Predicate k030799 (ABX MICROS 60)**
Intended Use	The **ABX MICROS ES 60** (OT and CT models) is a quantitative multi-parameter, automated hematology analyzer for in vitro diagnostic use in clinical laboratories to identify and enumerate the following parameters: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, PLT, MPV, LYM%, LYM#, MON%, MON#, GRA%, GRA#, in K2EDTA and K3EDTA anticoagulated venous whole blood samples of adult patient population. It is not intended to be used for pediatric subjects.	The **ABX MICROS 60 Hematology Analyzer** is a fully automated (microprocessor controlled) hematology analyzer used for the ***in vitro*** diagnostic testing of whole blood specimens or blood cell concentrates. It operates in complete blood count (CBC) mode.
Principles of Measurement		
RBC, PLT, HCT, MPV	Impedance	Same
HGB	Spectrophotometry	Same
WBC, WBC Differential (LYM, MON, GRA))	Impedance	Same
RDW, MCV, MCH, MCHC	Calculation	Same
Reagents		
Diluent	ABX Minidil LMG	Same
Lyse	ABX Minilyse LMG or ABX Alphalyse 360	Same
Cleaner	ABX Miniclean	Same
Reagent Pack	ABX Minipack LMG	Same
Concentrated cleaning reagent	ABX Minoclair	Same
Quality Controls	ABX Minotrol 16 (3 levels)	Same
Calibrator	ABX Minocal	Same
System configuration	Bench top	Same

Item	**Candidate (ABX MICROS ES 60)**	**Predicate k030799 (ABX MICROS 60)**
	Handheld barcode reader (optional) Integrated barcode reader (CT version only) Printer	
Sampling mechanism	Single tube presentation – open and closed vial sampling	Same
Aspiration pathway	Single sampling probe and common aspiration pathway used for all sample presentation modes	Same
Minimum Sample Volume **Specimen sample volume**	50 µL 10 µL	Same Same
Counting aperture diameters **RBC/PLT** **WBC**	 50 µm 80 µm	 Same Same
Dilution ratios		
RBC/PLT chamber	1/15000	Same
Performance claims		
Precision		
WBC	< 2.5 %	Same
RBC	< 2.0 %	Same
HGB	< 1.5 %	Same
HCT	< 2.0 %	Same
PLT	< 5.0 %	Same
Accuracy		
WBC	$R^2 > 95\%$	Same
RBC	$R^2 > 95\%$	Same
HGB	$R^2 > 95\%$	Same
HCT	$R^2 > 95\%$	Same
PLT	$R^2 > 95\%$	Same

6.3 Comparison with predicate Device : Differences

Item	**Candidate (ABX MICROS ES 60)**	**Predicate k030799 (ABX MICROS 60)**
User Interface Display	Automated instrument with 8" LCD touch screen display	Automated instrument with 3" LCD display
Software application	Linux-based software application	Internally developed software application
Analytical cycle	1) Draining sequence done by vacuum 2) No air bubble.	1) Draining sequence movement 2) Presence of air bubble at the end of all cycles

Item	**Candidate (ABX MICROS ES 60)**	**Predicate k030799 (ABX MICROS 60)**
Sample types	Whole blood samples only	Whole blood samples and blood cell concentrates
Dilution ratios		
WBC chamber	1/260	1/250
Throughput	OT / CT models: 60 / 50 samples per hour	OT / CT model: approx. 60 / 55 samples per hour
Dimensions	OT / CT models: 43 x 36 x 36 cm	OT / CT models:44 x 36 x 33 cm
Weight	OT model: 14 kg CT model: 17 kg	OT model: 14 kg CT model: 14 kg
Performance claims		
High Linearity limit		
WBC (10^3/mm^3)	100	Same
RBC (10^6/mm^3)	8.0	Same
HGB (g/dL)	24	26
HCT (%)	70	80
PLT (10^3/mm^3)	2200	Same
Limit Of Quantitation		
WBC (10^3/mm^3)	0.8	Not available
RBC (10^6/mm^3)	0.7	Not available
HGB (g/dL)	0.6	Not available
HCT (%)	8.0	Not available
PLT (10^3/mm^3)	42	Not available
Carry-over		
WBC	< 1%	< 0.5%
RBC	< 1%	< 0.5%
HGB	< 1%	< 0.5%
PLT	< 1%	< 0.5%

7.0 Special Control/Guidance Document Referenced :

7.1 Standards Followed

- **CLSI EP05-A2:** Evaluation of Precision Performance of Quantitative Measurement Methods – 2004
- **CLSI EP06-A:** Evaluation of the Linearity of Quantitative Measurement Procedure: A Statistical Approach – 2003
- **CLSI EP07-A2:** Interference Testing in Clinical Chemistry – 2005
- **CLSI EP09-A3:** Measurement Procedure Comparison and Bias Estimation Using Patient Samples – 2013
- **CLSI EP17-A2:** Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures – 2012
- **CLSI EP28-A3c:** Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory – 2008

- **CLSI H20-A2:** Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods – 2007
- **CLSI H26-A2:** Validation, Verification and Quality Assurance of Automated Hematology Analyzers – 2010
- **IEC61010-1, IEC61010-2-081, IEC61010-2-101, UL61010-1, CAN/CSA-C22.2 No. 61010-1-12, CAN/CSA-C22.2 No. 61010.2.081-04, CAN/CSA-C22.2 No. 61010-2-101-04:** Safety requirements for electrical equipment for measurement, control, and laboratory use
- **EN61326-1, EN61326-2-6:** Electrical equipment for measurement, control and laboratory use - EMC requirements
- **ISO14971:** Medical devices – Application of risk management to medical devices

7.2 FDA Guidances Followed

- Guidance for Industry and FDA Staff : Format for Traditional and Abbreviated 510(k)s - 2005
- Final Guidance for Industry and FDA: Class II Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells – 2001
- Guidance for Industry and FDA Staff : Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices – 2005
- Guidance for Industry, FDA Reviewers and Compliance on Off-The-Shelf Software Use in Medical Devices – 1999
- Draft Guidance for Industry and Food and Drug Administration Staff on the Content of Premarket Submissions for Management of Cybersecurity in Medical Devices - 2013

8.0 Summary of Performance Data :

8.1 Analytical Performance

8.1.1 Analytical Limits at Low Level

Limit of Blank (LoB)

Plasma samples, obtained by centrifugation of normal samples, were used as blank samples, in order to be as close as possible as the blood sample matrix.
To estimate the LoB, a total of 60 repeated measurements of different plasma are run in the same series (5 different samples run 12 times).
This test is performed on 2 instruments with two reagents lots.
Results on Micros ES60 OT and Micros ES60 CT were similar and met specifications.

LoB obtained from 60 repeated measurements of 5 different plasma samples, are:

Measurand	LoB
WBC	$0.1x10^3/mm^3$
RBC	$0.01x10^6/mm^3$
HCT	0.1 %
PLT	$1x10^3/mm^3$

Limit of Detection (LoD)

A set of six samples with very low parameter concentration (i.e. in the range LoB and 4 x LoB) are run 10 times over several days.
To estimate the LOD, take 60 results and calculate the pooled standard deviation (SDs).
This test is performed on 2 instruments with two reagents lots.
Results on Micros ES60 OT and Micros ES60 CT were similar and met specifications.

LoD obtained from 10 runs of 6 low samples on each instrument are:

Measurand	LoD
WBC	$0.2x10^3/mm^3$
RBC	$0.01x10^6/mm^3$
HGB	0.5 g/dL
HCT	0.2 %
PLT	$4x10^3/mm^3$

Limit of Quantitation (LoQ)

To estimate the limit of quantitation, several ranges of linearity in low concentrations are prepared. Between 3 to 6 samples by level are prepared and run at least 5 times each, 40 replicates by level are necessary. The LoQ data are considered acceptable when the %Total-error is smaller than the desired total error for each measurand.

This test is performed on 2 instruments with two reagents lots.
Results on Micros ES60 OT and MicrosES60 CT were similar and passed acceptance limits.

LoQ obtained from at least 40 runs of 4 samples by level are:

Measurand	LoQ
WBC	$0.8x10^3/mm^3$
RBC	$0.7x10^6/mm^3$
HGB	0.6 g/dL
HCT	8%
PLT	$42x10^3/mm^3$

8.1.2 Precision(Repeatability/Reproducibility)

Imprecision (Repeatability)

Repeatability was performed using 12 normal and 10 abnormal fresh whole blood samples collected into tubes containing K2EDTA anticoagulant. Each sample was run 10 consecutive times on two models of the Micros ES60 (ES60 OT and ES 60 CT), in a single day and all runs were completed within 8 hours of sample collection.
The size of the standard deviation was compared with the mean value of each parameter. This standard deviation divided by the mean is known as the Coefficient of Variation (CV) and is expressed as a percentage: CV% = (100*[Standard Deviation/Mean])

The results obtained were in the specifications.

Precision (Repeatability) Acceptance Criteria

	WBC	RBC	HGB	HCT	PLT	LYM%	MON%	GRA%
%CV	<2.5	<2	<1.5	<2	<5	<10	<20	<4

Imprecision (Reproducibility)

Reproducibility was assessed on three Micros ES60 instruments at three sites, each with its own operator. On each site; High, Normal, and Low levels of one single lot of Minotrol control material were run in duplicate, twice each day, during a minimum of 18 days.
Total standard deviation and CV% were calculated for each measurand and results obtained were in the specifications.

Precision (Reproducibility) Acceptance Criteria

Acceptable Total CV Claim (%)	Low Level Control	Normal Level Control	High Level Control
WBC	7.0	5.0	4.0
RBC	4.0	3.0	3.0
HGB	5.0	4.0	3.0
HCT	5.0	4.5	4.0
MCV	4.0	3.0	2.5
MCH	7.0	4.5	4.0
MCHC	7.0	4.5	4.0
RDW	5.0	5.0	5.0
PLT	15.0	10.5	7.0
LYM%	8.0	8.0	8.0
MON%	15.0	14.0	11.0
GRA%	12.0	4.0	3.0
LYM#	8.0	8.0	8.0
MON#	15.0	14.0	11.0
GRA#	12.0	4.0	3.0

8.1.3 Linearity / Assay's Measuring (Reportable) Range

Commercial High and Full Range Linearity kits were used to perform the linearity studies. The expected values of the kit samples were considered the "true values". Each level was run in replicates of four (n=4) as recommended by the kit supplier. For each level, the 4 replicate results were plotted versus the theoretical value. The findings of the polynomial regression analysis indicate that the ABX Micros ES 60 exhibits linearity across the claimed range.

The Analytical Measuring Range is defined as the range comprised between the Limit of Quantitation and the High Linearity Limit determined for each parameter.
The claimed AMR are therefore:

Parameter	AMR on Micros ES60
WBC ($10^3/mm^3$)	0.8 - 100
RBC ($10^6/mm^3$)	0.7 - 8
PLT ($10^3/mm^3$)	42 - 2200
HGB (g/dL)	0.6 - 24.0
HCT (%)	8.0 - 70.0

8.1.4 Carryover

The potential for sample carryover was tested in duplicate on the ABX Micros ES 60 OT and CT instruments using alternating high and low concentrations samples.

The percentage of carryover is calculated using the formula below:

$$Ct\% = \frac{low4 - low6}{high3 - low6} \times 100$$

All carry-over results are within specifications for the ABX Micros ES OT and CT Systems.

	Carry-over Limit (%CV)
WBC	<1%
RBC	<1%
HGB	<1%
PLT	<1%

8.1.5 Interfering substances

The interference effect is evaluated following two methodologies:

- By addition : evaluating the effect of potentially interfering substances added to the sample of interest:

A potential interfering substance is added to a sample and the bias relative to a control portion of the sample is evaluated ("paired-difference testing"). This bias was compared to the acceptance criteria.
For all tests performed with the following potential interferents, the bias remained below the acceptable limit and therefore, no significant interference was observed: urea, bilirubin, lipemia, and hemolysis.
An interference on WBC counts has been observed in presence of yeast in the sample.

- By comparison: evaluating the bias of individual specimen:

Representative patient specimens and a control sample (without interferent) are run in duplicate in comparison to a comparative measurement procedure (Micros 60). Then the bias versus comparative measurement values was plotted for each specimen group. Both measurement procedures had 10 to 20 samples in each group to demonstrate sufficient precision.
A comparable effect was observed on the ABX Micros ES 60 and the reference device for the interferences from: WBC fragments, Myelocytes, nucleated RBC, RBC Inclusion, RBC Agglutinins / Cold Agglutinins / RBC Rouleaux, Dual RBC population, RBC fragments, Target cells, Platelet Aggregates, Platelet Satelitism, Macrothrombocytes / Large Platelets, Small RBC Leukocytosis.

Additionnally, Megakaryoctes and Parasites are potential interferents on respectively WBC and Monocytes counts that could not be tested, but that are well described in literature.

8.1.6 Sample stability

11 whole venous blood specimens (collected in K2EDTA and K3EDTA) were analyzed on the ABX Micros ES 60 (OT model) at one site in France. Following the collection (T0), each specimen was divided in half, with one sample stored at ambient temperature (20-24^{o}C) and the other stored under refrigerated conditions (2-8^{o}C). Testing for stability was performed at 2, 6, 8, 10, 24, 36, 48, 60 and 72 hours after T0. The first aliquot of each specimen was run sequentially in any order. The second aliquot was run in reverse order to minimize the effects of carryover and drift. The acceptance criteria for sample stability is given as an acceptable maximum bias of the value at T with the value at T0.
All data passed specifications.

Parameters	Sample stability when stored refrigerated (2-8°C)	Sample stability when stored at room temperature (20-24°C)
WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT	48 hours	36 hours
RDW	36 hours	10 hours
MPV	24 hours	24 hours
LYM%, LYM#, MON%, MON#, GRA%, GRA#,	24 hours	8 hours

8.2 Other supportive performance data using clinical specimens

In order to support the equivalence and comparability claims made for the ABX Micros ES 60 in vitro diagnostic hematology analyzer, some performance studies were done in external clinical laboratories with clinical blood specimens collected prospectively or not. These may be considered as “Clinical studies”.

8.2.1 Comparability with Predicate Device

A total of 179 whole blood specimens from adult patients were analyzed at four test sites in the US.
Each of the samples was analyzed in duplicate on the ABX Micros ES 60 (CT model) and on the predicate ABX Micros 60.
Bias was estimated at three points for each parameter: the low end of the distribution of observations, the mid-point, and the high end of the distribution. Bias was estimated separately for each replicate. Acceptance criteria were met for all measurands at all levels. These findings support the claim that the ABX Micros ES60 candidate device and the ABX Micros 60 predicate device are substantially equivalent, and demonstrate acceptable levels of bias.

8.2.2 Comparability between Sampling methods

A total of 237 whole blood specimens from adult patients were analyzed at one test site in France.
Each of the samples was analyzed in duplicate on the ABX Micros ES 60 CT (Close Tube model) and on the ABX Micros ES 60 OT (Open Tube model).

Bias was estimated at three points for each parameter: the low end of the distribution of observations, the mid-point, and the high end of the distribution. Bias was estimated separately for each replicate. Acceptance criteria were met for all measurands at all levels. These findings support the claim that both Open Tube and Close Tube models of ABX Micros ES60 device yield comparable performances across the analytical range for all the parameters.

8.2.3 Comparability between Anticoagulant types

A total of 52 normal and pathological blood specimens were analyzed on the ABX Micros ES60 (CT model) at three sites in the US. Different instruments and operators were used at each site. The specimens used in this study were venous blood specimens that were prospectively collected for this study specifically. Each subject provided blood collected in both K2EDTA and K3EDTA.
Each of the samples was analyzed in duplicate on the ABX Micros ES 60.
Bias was estimated at three points for each parameter: the low end of the distribution of observations, the mid-point, and the high end of the distribution. Bias was estimated separately for each replicate. Acceptance criteria were met for all measurands at all levels. These findings support the claim that K2EDTA and K3EDTA specimens give comparable results as measured on the ABX Micros ES60 hematology analyzer.

8.2.4 Clinical Sensitivity / Specificity

100 normal and 100 pathological samples preserved in K2EDTA covering the full analytic range of the ABX Micros ES60 were analyzed in duplicate on the ABX Micros ES60 (CT model) and ABX Micros ES60 (OT model). Samples used for this study were left-over samples from both hospital and private independent clinical laboratories in France. Two slides with May Grünwald Giemsa staining were prepared for each sample. Slide reviews were conducted as a gold standard reference and WBC differential counts were conducted using 400-cell reference differential count (200 cells per reader, 2 readers) on each sample following the procedure discussed in CLSI H20-A2.
Samples were classified into Normal or Abnormal samples for the ABX Micros ES60 OT, ABX Micros ES60 CT, and the reference method (manual slide microscopy for differential count and morphological appreciation; the predicate ABX Micros 60 for quantitative CBC parameters). Abnormal samples were subdivided into those with abnormal proportions of one or more cell types (quantitative), and those containing abnormal cells (morphological).
Method comparison studies were designed using the CLSI H20-A2 procedure by the construction of the “envelope” that takes into account the imprecision of both the test and the manual method (95% and 99% confidence interval respectively).
The ability to identify abnormal samples and listed pathologies was evaluated according the CLSI H20-A2 by creating predictive value tables for distributional and morphological classification. From these tables, the efficiency, sensitivity, specificity, positive predictive value, and negative predictive value were calculated.
For each cell type, the mean of the manual differential count is compared with the mean of the analyzer count.
For WBC differential count analysis, the scatter plot of the means of the test method (yi) vs. the means of the reference method (xi) for each sample (i) is traced. On each scatter

plot, the 95% and 99% confidence intervals that take into account the imprecision of the test and reference methods are drawn.
The ABX Micros ES60 OT and CT models have shown acceptable performances in detecting an abnormal sample with good sensitivity. Positive predictive and negative predictive values are acceptable. Moreover, the WBC differential analysis comparison between the Micros ES60 and the manual microscopy slide observations (Gold Standard) show acceptable results. The data demonstrate the accuracy of the ABX Micros ES60 performance.

8.2.5 Reference Interval

275 (135 male and 140 female) normal adult samples (whole blood samples collected in K2EDTA) were analyzed in duplicate on the ABX Micros ES60 (OT model) and ABX Micros ES60 (CT model) at one test site in the US.
The nonparametric data analysis method was used, depending only on the ranks of the reference data arranged in order of increasing size. Per EP28-A3, the reference interval is determined to be between and including the lower and upper reference limits, which enclose 95% of the values from the reference population subjects. Confidence intervals for the reference limit were calculated using a 90% probability (90% CI).

Defined reference values are not significantly different between the ABX Micros ES60 OT and CT models. For each gender, a single reference interval applicable (Shared Interval) on both versions of the analyzers has been defined as described in the following table.

MICROS ES60 Reference Interval	MALES (N=135)		FEMALES (N=140)	
	LOW	HIGH	LOW	HIGH
WBC ($10^3/mm^3$)	4.3	9.6	4.2	10.3
RBC ($10^6/mm^3$)	4.1	5.7	4.0	5.1
HGB (g/dl)	12.6	16.7	11.6	15.1
HCT (%)	38.3	50.8	35.8	46.4
MCV (μm^3)	83	97	83	98
MCH (pg)	26.7	32.3	26.8	32.5
MCHC (g/dl)	31.7	34	31.8	34.0
RDW (%)	11.1	14.4	11.3	13.9
PLT ($10^3/mm^3$)	156	370	181	393
MPV (μm^3)	6.3	9.1	6.5	9.0
LYM ($10^3/mm^3$)	1.1	3.1	1.2	3.4
MON ($10^3/mm^3$)	0.1	0.6	0.1	0.6
GRA ($10^3/mm^3$)	2.6	7.0	2.7	7.4
%LYM (%)	16.5	44.7	17.7	45.2
%MON (%)	3.1	8.3	3.3	8.1
%GRA (%)	49.1	76.9	49.2	77.7

Reference intervals have been established on ABX Micros ES60 OT and CT for each parameter, based on a CLSI EP28-A3 study. These intervals are given in the labeling of the Micros ES60.
However, expected values will vary with sample population and/or geographical location. Horiba highly recommends that each laboratory establishes its own normal ranges based upon its local population.

9.0 Proposed Labeling :

The labeling is written as per the recommendations given in standard EN18113-2. It takes into account the requirements of 21 CFR Part 809.10.

10.0 Conclusion :

As per 21CFR Part §807.92(b)(3), the nonclinical and clinical tests demonstrate that the ABX Micros ES 60 device is as safe, as effective, and performs as well as or better than the predicate device .

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.